ask Betsey Kemmerer

L11 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003169191 MEDLINE
DOCUMENT NUMBER: 22573537 PubMed ID: 12687003
TITLE: The BMP antagonist noggin regulates cranial suture fusion.
AUTHOR: Warren Stephen M; Brunet Lisa J; Harland Richard M; Economides Aris N; Longaker Michael T
CORPORATE SOURCE: Department of Surgery, Stanford University School of Medicine, Stanford, California 94305-5148, USA.
SOURCE: NATURE, (2003 Apr 10) 422 (6932) 625-9.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030416
Last Updated on STN: 20030501
Entered Medline: 20030430

AB During skull development, the cranial connective tissue framework undergoes intramembranous ossification to form skull bones (calvaria). As the calvarial bones advance to envelop the brain, fibrous sutures form between the calvarial plates. Expansion of the brain is coupled with calvarial growth through a series of tissue interactions within the cranial suture complex. Craniosynostosis, or premature cranial suture fusion, results in an abnormal skull shape, blindness and mental retardation. Recent studies have demonstrated that gain-of-function mutations in fibroblast growth factor receptors (fgfr) are associated with syndromic forms of craniosynostosis. Noggin , an antagonist of bone morphogenetic proteins (BMPs), is required for embryonic neural tube, somites and skeleton patterning. Here we show that noggin is expressed postnatally in the suture mesenchyme of patent, but not fusing, cranial sutures, and that noggin expression is suppressed by FGF2 and syndromic fgfr signalling. Since noggin misexpression prevents cranial suture fusion in vitro and in vivo, we suggest that syndromic fgfr-mediated craniosynostoses may be the result of inappropriate downregulation of noggin expression.

L11 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003192289 MEDLINE
DOCUMENT NUMBER: 22597394 PubMed ID: 12710966
TITLE: BMP signals regulate Dlx5 during early avian skull development.
AUTHOR: Holleville Nicolas; Quilhac Alexandra; Bontoux Martine; Monsoro-Burq Anne Helene
CORPORATE SOURCE: Institut d'Embryologie Cellulaire et Moleculaire, CNRS, UMR 7128, 49 bis, avenue de La Belle Gabrielle, 94736, Nogent-sur-Marne, France.
SOURCE: DEVELOPMENTAL BIOLOGY, (2003 May 1) 257 (1) 177-89. Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030425
Last Updated on STN: 20030604
Entered Medline: 20030603

AB The vertebrate skull vault forms almost entirely by the direct mineralisation of mesenchyme, without the formation of a cartilaginous template, a mechanism called membranous ossification. Dlx5 gene mutation leads to cranial dismorphogenesis which differs from the previously studied craniosynostosis syndromes [Development 126 (1999), 3795; Development 126 (1999), 3831]. In avians, little is known about the genetic regulation of cranial vault development. In this study, we analyze Dlx5 expression and regulation during skull formation in the chick embryo. We compare Dlx5 expression pattern with that of several genes involved in mouse cranial suture regulation. This provides an initial description of the expression in the developing skull of the genes encoding the secreted molecules BMP 2, BMP 4, BMP 7, the transmembrane FGF receptors FGFR 1, FGFR 2, FGFR 4, the transcription factors Msx1, Msx2, and Twist, as well as Goosecoid and the early membranous bone differentiation marker osteopontin. We show that Dlx5 is activated in proliferating osteoblast precursors, before osteoblast differentiation. High levels of Dlx5 transcripts are observed at the osteogenic fronts (OFs) and at the edges of the suture mesenchyme, but not in the suture itself. Dlx5 expression is initiated in areas where Bmp4 and Bmp7 genes become coexpressed. In a calvarial explant culture system, Dlx5 transcription is upregulated by BMPs and inhibited by the BMP-antagonist Noggin. In addition, FGF4 activates Bmp4 but not Bmp7 gene transcription and is not sufficient to induce ectopic Dlx5

expression in the immature calvarial mesenchyme. From these data, we propose a model for the regulatory network implicated in early steps of chick calvarial development.

L11 ANSWER 1 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2003257195 MEDLINE
DOCUMENT NUMBER: 22666840 PubMed ID: 12782679
TITLE: Selective inhibitors of the osteoblast proteasome stimulate bone formation in vivo and in vitro.
AUTHOR: Garrett I R; Chen D; Gutierrez G; Zhao M; Escobedo A; Rossini G; Harris S E; Gallwitz W; Kim K B; Hu S; Crews C M; Mundy G R
CORPORATE SOURCE: OsteoScreen Inc, San Antonio, Texas 78229, USA.. garrett@osteoscreen.com
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (2003 Jun) 111 (11) 1771-82.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030604
Last Updated on STN: 20030713
Entered Medline: 20030711
AB We have found that the ubiquitin-proteasome pathway exerts exquisite control of osteoblast differentiation and bone formation in vitro and in vivo in rodents. Structurally different inhibitors that bind to specific catalytic beta subunits of the 20S proteasome stimulated bone formation in bone organ cultures in concentrations as low as 10 nM. When administered systemically to mice, the proteasome inhibitors epoxomicin and proteasome inhibitor-1 increased bone volume and bone formation rates over 70% after only 5 days of treatment. Since the ubiquitin-proteasome pathway has been shown to modulate expression of the Drosophila homologue of the bone morphogenetic protein-2 and -4 (BMP-2 and BMP-4) genes, we examined the effects of noggin, an endogenous inhibitor of BMP-2 and BMP-4 on bone formation stimulated by these compounds and found that it was abrogated. These compounds increased BMP-2 but not BMP-4 or BMP-6 mRNA expression in osteoblastic cells, suggesting that BMP-2 was responsible for the observed bone formation that was inhibited by noggin. We show proteasome inhibitors regulate BMP-2 gene expression at least in part through inhibiting the proteolytic processing of Gli3 protein. Our results suggest that the ubiquitin-proteasome machinery regulates osteoblast differentiation and bone formation and that inhibition of specific components of this system may be useful therapeutically in common diseases of bone loss.

L8 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:13742 CAPLUS
DOCUMENT NUMBER: 136:180879

TITLE: Noggin and retinoic acid transform the identity of avian facial prominences

AUTHOR(S): Lee, S.-H.; Fu, K. K.; Hul, J. N.; Richman, J. M.
CORPORATE SOURCE: Department of Oral Health Science, Faculty of Dentistry, University of British Columbia, Vancouver, BC, V6T 1Z3, Can.

SOURCE: Nature (London, United Kingdom) (2001), 414(6866), 909-912
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The signals that det. body part identity in vertebrate embryos are largely unknown, with some exceptions such as those for teeth and digits. The vertebrate face is derived from small buds of tissue, facial prominences, that surround the embryonic oral cavity. In chicken embryos, the skeleton of the upper beak is derived from the frontonasal mass and maxillary prominences. Here bone morphogenetic proteins (Bmps) and the vitamin A deriv., retinoic acid (RA), are used to specify the identity of the frontonasal mass and maxillary prominences. Implanting two beads adjacent to the stage-15 presumptive maxillary field, one soaked in the Bmp antagonist Noggins and one soaked in RA, induces a duplicate set of frontonasal mass skeletal elements in place of maxillary bones. The authors also show that the duplicated beak is due to transformation of the maxillary prominence into a second frontonasal mass and not due to ectopic migration of cells or splitting of the normal frontonasal mass. Thus the levels of Bmp and RA det. whether specific regions of the face form maxillary or frontonasal mass derivs.

L8 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:142419 CAPLUS
DOCUMENT NUMBER: 134:293233

TITLE: Expression of noggin gene during development of maxillofacial region in mice

AUTHOR(S): Inage, Toshihiko; Nakata, Tomoko; Kamogawa, Daisuke; Sekiguchi, Yutaka; Sato, Michitomo; Ono, Masaru; Kamogawa, Hiroyuki; Sekiwa, Tadanobu; Terakado, Masaaki; Kuwata, Fumiyuki; Sato, Yoshinori; Oida, Shinichirou

CORPORATE SOURCE: Department of Anatomy, Nihon University School of Dentistry, Kanda-Surugadai, Chiyoda-ku, Tokyo, 101-8310, Japan

SOURCE: Shika Kiso Igakkai Zasshi (2000), 42(6), 563-572
CODEN: SHKKAN; ISSN: 0385-0137

PUBLISHER: Shika Kiso Igakkai

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB To verify the function of noggin in the hard tissue formation of embryogenesis, expressions of noggin mRNA were studied by in situ hybridization. In the early stage of somite formation, noggin mRNA appeared in the brain membrane and myotome around the sclerotome at the stage of E 11 days. Noggin mRNA was detected in the chondrogenic condensation with the formation of Meckel's cartilage. At the stage of calcification of Meckel's cartilage, chondrocytes at the resting stage and hypertrophic stage expressed intense mRNA. In the area of mandibular bone formation, the osteoblasts and subosteoblastic cells also showed an intense expression of noggin mRNA. The cells constituting periosteum expressed noggin mRNA intensively. The expression of noggin mRNA was obscure in the tooth germ at the cap stage except for in the mesenchymal cells of the dental follicle. In the tooth germ at postnatal 5 days, the dental papilla cells, periodontal ligament cells and osteoblasts at the bifurcation to root showed gene expression. During the development of skeletal cartilage, noggin mRNA was detected in chondrocytes at the resting stage, and the hypertrophic stage expressed intense mRNA. With ossification, the osteoblasts and subosteoblastic cells also showed an intense expression of noggin mRNA.

L11 ANSWER 6 OF 7 MEDLINE on STN
ACCESSION NUMBER: 1999124468 MEDLINE
DOCUMENT NUMBER: 99124468 PubMed ID: 9927278
TITLE: Skeletal bone morphogenetic proteins suppress the expression of collagenase-3 by rat osteoblasts.
AUTHOR: Gazzerro E; Rydziel S; Canalis E
CORPORATE SOURCE: Department of Research, Saint Francis Hospital and Medical Center, Hartford, Connecticut 06105-1299, USA.
CONTRACT NUMBER: AR-21707 (NIAMS)
SOURCE: ENDOCRINOLOGY, (1999 Feb) 140 (2) 562-7.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Space Life Sciences
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990223

AB Bone morphogenetic proteins (BMPs) are secreted by skeletal cells, induce the differentiation of mesenchymal cells into cells of the osteoblastic lineage, and increase their differentiated function. BMPs also decrease collagenase-3 expression by the osteoblast. We tested the autocrine role of BMPs on collagenase-3 expression in osteoblast-enriched cells from fetal rat calvariae (Ob cells) by examining the effects of noggin, a specific inhibitor of BMP binding and function. Although collagenase-3 transcript expression declined in untreated Ob cells in culture over a 24-h period, BMP-2, -4, and -6 decreased collagenase-3 messenger RNA levels in cells treated for 2-24 h. The addition of noggin prevented the decrease of collagenase-3 transcripts in control cultures, opposed the inhibitory actions of BMP-2, and increased the levels of the protease in the culture medium. Noggin did not alter the decay of collagenase-3 messenger RNA in transcriptionally arrested cells, and it increased the levels of collagenase-3 heterogeneous nuclear RNA in Ob cells. In conclusion, noggin enhances the synthesis of collagenase-3 in osteoblasts, supporting the notion that BMPs act as autocrine suppressors of collagenase-3 in skeletal cells, an effect that may contribute to the maintenance of the bone matrix.

L11 ANSWER 7 OF 7 MEDLINE on STN
ACCESSION NUMBER: 1999072832 MEDLINE
DOCUMENT NUMBER: 99072832 PubMed ID: 9854046
TITLE: Bone morphogenetic proteins induce the expression of noggin, which limits their activity in cultured rat osteoblasts.
AUTHOR: Gazzerro E; Gangji V; Canalis E
CORPORATE SOURCE: Departments of Research and Medicine, Saint Francis Hospital and Medical Center, Hartford, Connecticut 06105; and The University of Connecticut School of Medicine, Farmington, Connecticut 06030, USA.
CONTRACT NUMBER: AR21707 (NIAMS)
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1998 Dec 15) 102 (12) 2106-14.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990201

AB Bone morphogenetic proteins (BMPs) induce the differentiation of cells of the osteoblastic lineage and enhance the function of the osteoblast. Growth factors are regulated by binding proteins, but there is no information about binding proteins for BMPs in skeletal cells. Noggin specifically binds BMPs, but its expression by cells of the osteoblastic lineage has not been reported. We tested for the expression of noggin and its induction by BMP-2 in cultures of osteoblast-enriched cells from 22-d-old fetal rat calvariae (Ob cells). BMP-2 caused a time- and dose-dependent increase in noggin mRNA and polypeptide levels, as determined by Northern and Western blot analyses. The effects of BMP-2 on noggin transcripts were dependent on protein, but independent of DNA synthesis. BMP-2 increased the rates of noggin transcription as determined by nuclear run-on assays. BMP-4, BMP-6, and TGF-beta1 increased noggin mRNA in Ob cells, but basic fibroblast growth factor, platelet- derived growth factor BB, and IGF-I did not. Noggin decreased the stimulatory effects of BMPs on DNA and collagen synthesis and alkaline phosphatase activity in Ob cells. In conclusion, BMPs induce noggin transcription in Ob cells, a probable mechanism to limit BMP action in osteoblasts.